



PCT

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference R2647-PCT		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP 03/13327	International filing date (day/month/year) 26.11.2003	Priority date (day/month/year) 26.11.2002	
International Patent Classification (IPC) or both national classification and IPC B01J2/10			
Applicant UNIVERSITEIT GENT			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 7 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 27.04.2004		Date of completion of this report 07.04.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840		Authorized Officer Cubas Alcaraz, J Telephone No. +49 30 25901-324 	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/13327**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-34 as originally filed

Claims, Numbers

1-38 received on 05.02.2005 with letter of 03.02.2005

Drawings, Sheets

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2,5,7-15,17,19,21-25,27-32
	No: Claims	1,3,4,6,16,18,20,26,33-38
Inventive step (IS)	Yes: Claims	
	No: Claims	1-38
Industrial applicability (IA)	Yes: Claims	1-38
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

1. The following document is referred to in this communication:

D1: US-A-4416606

2. The present application does not meet the requirements of Article 33(1)(2) because the subject-matter of claims 1 and 3 is not new.

2.1 Document D1 describes a device for the wet granulation of material (col. 1, lines 5-9). The device comprises (cf. col. 3, line 5-col. 4, line 60; figures 1-5) a housing (reference 1 in the figures), inlet means for the mixture solid-liquid (reference 7 in the figures) and a twin screw system, comprising a first transport zone (reference I in the figures) an agglomeration zone (reference II₁ in the figures) and a second transport zone (reference II₂). It has to be pointed out that in the present application it is not specified how is the movement (forward or backward) in the second transport zone. A final zone is provided with means for breaking the agglomerates. These last means are not creating a pressure gradient at the outlet of the granulation device, as can be seen clearly in the figures, specially figures 2 and 5. It is obvious that the material inside the device of D1 must be continuously advanced in order to get the final product. Thus, all the elements of the apparatus as disclosed in claim 1 of the present application can be identified in the apparatus of D1. Accordingly, the subject-matter of claim 1 is not new.

2.2 The additional features of claim 3 are only optional. These optional features are also described in D1 (see figures 1-5). Thus, the subject-matter of claim 3 is not new.

3. Document D1 also discloses a process for preparing granules using the apparatus and including all the steps of claim 16, which is therefore not new (Article 33 PCT).

4. Moreover, the disclosure of D1 anticipates the features of dependent claims 4, 6, 18, 20 and 26. Thus, the subject-matter of these claims is not new (Article 33).

5. Claims 33-38 are directed to the granules prepared using the apparatus and/or method of the previous claims, and shaped articles prepared using those granules. Since the apparatus and the method are not new, the granules cannot be considered as new. Furthermore, it has to be noted that, as advantages of the claimed apparatus and method, only economic reasons (less liquid, simple apparatus) are cited. There are no specific characteristics of the granules prepared using the claimed apparatus or method and therefore it is impossible to distinguish the granules prepared according to

the claimed invention from similar granules prepared using a different apparatus or method. Same reasoning applies to the articles prepared using those granules.

6. The dependent claims 2, 5, 7-15, 17, 19, 21-25 and 27-33 do not appear to contain any feature which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step (Article 33(1)(3)).

CLAIMS

1. An apparatus for the continuous wet granulation of a powder material, comprising:
 - 5 - a barrel having a granulation chamber provided between a first part (B) and a second part (B') of said barrel, the first part (B) being provided with at least one first inlet (1) connected with said granulation chamber for receiving said powder material and for supplying it to said granulation chamber and with at least one second inlet (2) connected
10 with said granulation chamber for receiving a granulating liquid and for supplying it to said granulation chamber, said granulation chamber having an aperture (9) for discharge of granules from said barrel, and
 - at least one continuously operated transporting means (S) provided in
15 said granulation chamber for continuously advancing said powder material toward the end of said granulation chamber while granulating said powder material with the aid of said granulating liquid, each said transporting means (S) comprising at least a first transport zone (4) at its rear end, an agglomeration zone (5) downstream from the first transport zone (4) for effecting particle size enlargement of said powder
20 material and contributing to advancing said powder material through said transporting means (S), and a second transport zone (8) at its front end, said at least one first inlet (1) and said at least one second inlet (2) of the barrel being positioned above the at least one first transport zone (4) of each said at least one transporting means (S),
 - 25 wherein said aperture (9) has a shape tightly fitting the terminal portion of said at least one transporting means (S) for directly discharging said granules from the granulation chamber without developing a pressure gradient at the exit of the granulation chamber.
- 30 2. An apparatus according to claim 1, characterised in that each said at least one transporting means (S) further comprises one or more additional transport zones (6, 8) and one or more additional agglomeration zones (7),

each agglomeration zone (5, 7) being positioned between two transport zones (4, 6, 8).

3. An apparatus for the continuous wet granulation of a powder material,
5 consisting essentially of:

- a barrel having a granulation chamber provided between a first part (B) and a second part (B') of said barrel, the first part (B) being provided with at least one first inlet (1) connected with said granulation chamber for receiving said powder material and for supplying it to said granulation chamber and with at least one second inlet (2) connected with said granulation chamber for receiving a granulating liquid and for supplying it to said granulation chamber, said granulation chamber having an aperture (9) for discharge of granules from said barrel, and
- at least one continuously operated transporting means (S) provided in
15 said granulation chamber for advancing said powder material toward the end of said granulation chamber while granulating said powder material with the aid of said granulating liquid, each said transporting means (S) comprising at least a first transport zone (4) at its rear end and optionally one or more additional transport zones (6), an
20 agglomeration zone (5) downstream from the first transport zone (4) and optionally one or more additional agglomeration zones (7), and a second transport zone (8) at its front end, each agglomeration zone (5, 7) being positioned between two transport zones (4, 6, 8), said at least one first inlet (1) and said at least one second inlet (2) of the barrel
25 being positioned above the at least one first transport zone (4) of each said at least one transporting means (S),

wherein said aperture (9) has a shape tightly fitting the terminal portion of said at least one transporting means (S) for directly discharging said granules from the granulation chamber without developing a pressure
30 gradient at the exit of the granulation chamber.

4. An apparatus according to claim 3, characterised in that said transporting means (S) is a rotating transporting means.

5. An apparatus according to claim 3 or claim 4, characterised in that said transporting means (S) is a single screw.
- 5 6. An apparatus according to claim 3 or claim 4, characterised in that said transporting means (S) is a twin screw.
7. An apparatus according to claim 5 or claim 6, characterised in that the length to diameter ratio of each screw is within a range from about 15 to
10 about 60.
8. An apparatus according to any of claims 3 to 7, characterised in that the cumulative lengths of the agglomeration zones (5, 7) represent from about 8% to about 30% of the length of the transporting means (S).
15
9. An apparatus according to any of claims 3 to 8, characterised in that the cumulative lengths of the agglomeration zones (5, 7) represent from about 10% to about 25% of the length of the transporting means (S).
- 20 10. An apparatus according to any of claims 3 to 9, characterised in that the respective dimensions of the first inlet (1) for receiving the powder material and of the second inlet (2) for receiving the granulation liquid are such that the weight ratio of the granulating liquid to the powder material is not above 16:100.
25
11. An apparatus according to any of claims 3 to 10, characterised in that the respective dimensions of the first inlet (1) for receiving the powder material and of the second inlet (2) for receiving the granulation liquid are such that the weight ratio of the granulating liquid to the powder material is not
30 above 12:100.
12. An apparatus according to any of claims 3 to 11, characterised in that the respective dimensions of the first inlet (1) for receiving the powder material

and of the second inlet (2) for receiving the granulation liquid are such that the weight ratio of the granulating liquid to the powder material is not above 8:100.

- 5 13. An apparatus according to any of claims 3 to 12, characterised in that the respective dimensions of the first inlet (1) for receiving the powder material and of the second inlet (2) for receiving the granulation liquid are such that the weight ratio of the granulating liquid to the powder material is not below 2:100.
- 10 14. An apparatus according to any of claims 3 to 13, characterised in that the respective dimensions of the first inlet (1) for receiving the powder material and of the second inlet (2) for receiving the granulation liquid are such that the weight ratio of the granulating liquid to the powder material is not below
- 15 4:100.
15. A process for the continuous wet granulation of a powder material, comprising continuously operating an apparatus according to any of claims 3 to 14.
- 20 16. A process for the continuous wet granulation of a powder material, comprising the steps of :
- (a) feeding a powder material to a first transport zone (4) of at least one continuously operated transporting means,
- 25 (b) feeding a granulating liquid to said first transport zone (4) of said at least one continuously operated transporting means,
- (c) continuously advancing said powder material and said granulating liquid from said first transport zone (4) to an agglomeration zone (5) of said at least one continuously operated transporting means downstream of said first transport zone (4) for agglomerating said wet
- 30 powder material,
- (d) transporting said agglomerated material from said agglomeration zone (5) to a second transport zone (8) of said at least one continuously

operated transporting means downstream of said agglomeration zone
(5) for producing granules, and
(e) directly discharging said granules from said second transport zone (8)
of said at least one continuously operated transporting means without
5 submitting said granules to any pressure gradient.

17. A continuous wet granulation process according to claim 16, further
comprising the step of continuously advancing said agglomerated material
from said agglomeration zone (5) to said second transport zone (8) of said
10 at least one continuously operated transporting means through one or
more combinations of an additional intermediate transport zone (6)
followed by an additional intermediate agglomeration zone (7).

18. A continuous wet granulation process according to claim 16 or claim 17,
15 characterised in that said at least one continuously operated transporting
means is a rotating transporting means.

19. A continuous wet granulation process according to any of claims 16 to 18,
characterised in that said at least one continuously operated transporting
20 means is a single screw.

20. A continuous wet granulation process according to any of claims 16 to 18,
characterised in that said at least one continuously operated transporting
means is a twin screw.
25

21. A continuous wet granulation process according to any of claims 16 to 20,
characterised in that the residence time of said powder material in said at
least one continuously operated transporting means is in the range of
about 5 seconds to about 180 seconds.
30

22. A continuous wet granulation process according to any of claims 16 to 21,
characterised in that the residence time of said powder material in said at

least one continuously operated transporting means is in the range of about 20 seconds to about 60 seconds.

- 5 23. A continuous wet granulation process according to any of claims 16 to 22, characterised in that said powder material contains a biologically-active ingredient.
- 10 24. A continuous wet granulation process according to claim 23, characterised in that the content of said biologically-active ingredient in powder material is within a range from 0.1% by weight to 99% by weight.
- 15 25. A continuous wet granulation process according to claim 23 or claim 24, characterised in that said biologically-active ingredient is a poorly soluble drug belonging to Class II or Class IV of the Biopharmaceutical Classification System.
- 20 26. A continuous wet granulation process according to any of claims 16 to 22, characterised in that said powder material is selected from foodstuffs, catalysts, chemicals, fertilisers, detergents and mineral ores.
27. A continuous wet granulation process according to any of claims 16 to 26, characterised in that the amount of the said granulating liquid is from about 2% to about 16% by weight of the powder material.
- 25 28. A continuous wet granulation process according to any of claims 16 to 27, characterised in that the amount of the said granulating liquid is from about 4% to about 12% by weight of the powder material.
- 30 29. A continuous wet granulation process according to any of claims 16 to 28, being carried out at a temperature within a range from about 10°C to about 50°C.

30. A continuous wet granulation process according to any of claims 16 to 29, characterised in further comprising a granule drying step (f) subsequent to discharging step (e).
- 5 31. A continuous wet granulation process according to any of claims 16 to 30, characterised in further comprising a granule dry milling step subsequent to discharging step (e).
- 10 32. A continuous wet granulation process according to any of claims 23 to 25, characterised in that said powder material further contains one or more physiologically acceptable excipients.
- 15 33. A granule population obtained by operating an apparatus according to any of claims 3 to 14 or by performing a process according to any of claims 15 to 32.
34. A granule population according to claim 33, having an average size within a range from about 250 μm to about 1,000 μm .
- 20 35. A granule population according to claim 33 or claim 34, having an average size within a range from about 250 μm to about 700 μm .
- 25 36. A solid shaped article obtained from a granule population according to any of claims 33 to 35.
37. A solid shaped article according to claim 36, in the form of a tablet, a composite article or a capsule.
- 30 38. A solid shaped article according to claim 37, being a tablet obtained by compressing the said granule population.